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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/061,979	01/31/2002	Jeremy S. Lee	080129-000100US	2049

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EXAMINER	
MARVICH, MARIA	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/061,979	LEE ET AL.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/24/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/31/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS 4/22/02.*

DETAILED ACTION

Election/Restrictions

This office action is in response to a Response to a Restriction Requirement filed 12/24/03. Applicant's election without traverse of Group I (claims 1-4 and 6-22) is acknowledged. This group was mistakenly indicated as claims 1-4, 6-15 and 18-22. However, Group I should have indicated that it is inclusive of claims 1-4 and 6-22. Claims 1-22 are pending in this application, claim 5 has been withdrawn.

Information Disclosure Statement

An IDS filed 1/31/02 has been identified but the documents listed on the IDS have not been received. Cited US patents that were obtained from the USPTO were considered but the non-patent literature was not considered. Copies of each document that applicants want considered should be sent. An IDS filed 4/22/02 has been identified and the documents considered. The signed and initialed PTO Form 1449s have been mailed with this action.

Drawings

Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see enclosed form PTO-948.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 16 are vague and indefinite in that the metes and bounds of a "metal-containing nucleic acid expresses an antigenic protein" are unclear. Nucleic acid encodes proteins but does not express the proteins.

Claims 1-4 and 6-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) **Nature of invention**. The invention recites a method for using metal containing nucleic acid comprising two strands of nucleic acid, which are joined by hydrogen bonds and

interchelated with divalent metal cations for induction of a physiological response. The disclosure teaches that metal containing nucleic acid has the properties of electrical conductance as well as being nuclease resistant. The invention utilizes a combination of molecular biology and clinical techniques.

2) **Scope of the invention**. Base claim 1 recites a method of producing a physiological response by administering metal containing nucleic acid, which reads on a method of gene therapy. Specifically in claims 3-4 and 16-17, the physiological response upon M-DNA introduction into an animal is the induction of an immune response. The steps of gene therapy exacerbate a complex method.

3) **Number of working examples and guidance**. The specification teaches construction of metal containing nucleic acids in which divalent metal cations such as Ni^{2+}, Co^{2+} and Mg^{2+} are interchelated with the hydrogen bonded base pairs and coordinated to a nitrogen atom in one of the aromatic nitrogen containing aromatic bases. The metal containing nucleic acid has the property of electrical conductance by accepting electrons from an electron donor. It is taught that the M-DNA provides useful detection systems for the identification of PCR products, ligation reactions, for the detection of particular genomic sequences and to monitor presence of nucleic acid binding moieties in a sample. Furthermore, it is demonstrated that M-DNA is nuclease resistant and therefore it is proposed that the M-DNA can mediate physiological response *in vivo* such as to generate an immune response. Applicants demonstrate that the M-DNA is immunogenic by injecting Ni^{2+} containing M-DNA intraperitoneally into Balb/C mice. Mice immunized with M-DNA show antibody titres to M-DNA. The disclosure neither provides examples of using M-DNA to express antigenic protein nor teaches that the DNA specifically

disclosed in example 1 and used in examples 2-4 would transcribe normally. Without knowing the nature of the DNA, the ability to generate an immune response is highly unpredictable.

4) **State of Art**. The art of producing an immune response upon injection of naked DNA is an emerging art. Typically, the DNA encodes an antigenic determinant to which an immune response is mounted by the host system (Falo et al pages 1239-1240). The production of anti-DNA antibodies is seen in autoimmune disorders such as systemic lupus and occurs when the DNA is presented to the immune system and is in complex with carrier proteins (see Rekvig, page 1, column 3, paragraph 2).

5) **Unpredictability of the art**. The unpredictability of the invention is high due to the lack of recited methods and because the nucleic acid is completely unknown at the onset as the invention. Applicants disclose that BalbC mice are injected with M-DNA. However, neither the sequence nor the properties associated with the sequence are provided. The specification teaches that the M-DNA used to induce the immune response is nickel-containing DNA but the specific sequence is unknown. For previous experiments, 20 mer duplex and 54 mer duplex DNA is used to form M-DNA by addition of zinc. However, the components of the DNA that are essential for induction of an immune response either directly inducing anti-DNA antibodies or to encode antigenic determinants are not taught.

The unpredictability of using the claimed invention for use in humans is mitigated due to the lack of methods or processes disclosed in the specification. Many parameters must be addressed for *in vivo* use and yet there are no methods or means disclosed in the specification such as delivery methods for the introduction of the modified cells into humans, means of preparing the DNA for *in vivo* applications, which DNA to be used and means of transfection.

While *in vitro* and animal models have been provided as evidence of success of treatment, *in vitro* results rarely correlate well with *in vivo* clinical trial results in patients and have not translated into successful human therapies. It is not clear that reliance on experimental models accurately reflects the relative superiority or efficacy of the claimed therapeutic strategy and applicants present no disclosed or art recognized nexus between the xenograft and nude mice experimental models and the human disease state. "Although animal studies have suggested low toxicity and excellent efficacy, these investigation have been limited by the use of immuno-deficienct mice" (Meng and Deiry, p. 6, column 1).

6) **Summary**. The invention recites a method for the production of a physiological response in animals by administration of metal containing nucleic acids. In view of unpredictability of the art to which the invention pertains and the lack of established protocols and the inability to predict what sequence will function to induce an immune response: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be concluded that the skilled artisan would have had to have conducted undue, unpredictable experimentation in order to practice the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (571)-272-0774. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (571)-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maria B Marvich, PhD
Examiner
Art Unit 1636

March 4, 2004

GERRY LEFFERS
PRIMARY EXAMINER